```
=> file medline hcaplus biosis biotechds scisearch embase
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 16:56:45 ON 29 JUL 2004

FILE 'HCAPLUS' ENTERED AT 16:56:45 ON 29 JUL 2004
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FILE 'BIOTECHDS' ENTERED AT 16:56:45 ON 29 JUL 2004
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=> s dimethylallyl-cycloacetoacetyl-L-tryptophan synthase
L1            1 DIMETHYLALLYL-CYCLOACETOACETYL-L-TRYPTOPHAN SYNTHASE

=> d l1 ibib ab

L1    ANSWER 1 OF 1  BIOTECHDS COPYRIGHT 2004 THOMSON DERWENT/ISI on STN
ACCESSION NUMBER: 2000-12161  BIOTECHDS
TITLE:            Producing a polypeptide of interest such as a hormone or
                  enzyme, comprising cultivating a mutant of a parent
                  Aspergillus cell which produces less of at least one toxin of
                  interest compared to the parent cell under the same
                  conditions;
                     toxin-deficient Aspergillus oryzae production by
                     mutagenesis
AUTHOR:           Christensen B E; Mollgaard H; Kaasgaard S; Lehmbeck J
PATENT ASSIGNEE:  Novo-Nordisk
LOCATION:         Bagsvaerd, Denmark.
PATENT INFO:      WO 2000039322 6 Jul 2000
APPLICATION INFO: WO 1999-DK726 22 Dec 1999
PRIORITY INFO:    DK 1999-745 27 May 1999; DK 1998-1726 23 Dec 1998
DOCUMENT TYPE:    Patent
LANGUAGE:         English
OTHER SOURCE:     WPI: 2000-452411 [39]
AB    Protein production involves culturing a mutant of a parent Aspergillus
      sp. cell, and isolating the protein from the medium.  The mutant has a
      1st nucleotide sequence encoding the protein and produces less than 1
      toxin of interest than the parent Aspergillus cell when grown under same
      conditions.  Also claimed are: a toxin-deficient Aspergillus sp. mutant
      host cell useful for foreign protein production; obtaining a
      toxin-deficient Aspergillus sp.  mutant host cell by subjecting a parent
      cell to mutagenesis and screening for mutant cells with reduced or no
      production of the toxin; nucleic acid encoding dimethylallyl-
      cycloacetoacetyl-L-tryptophan-
      synthase comprising a defined 1,393 bp sequence (disclosed); an
      isolated dimethylallyl-cycloacetoacetyl-L-
      tryptophan-synthase obtained from Aspergillus oryzae
      having a defined 437 amino acid sequence; a method for obtaining
      toxin-deficient Aspergillus mutant host cell involving transforming a
      host cell with a sequence encoding a protein and a nucleic acid having a
      modification of at least one gene involved in biosynthesis or secretion
      of at least one toxin and identifying the mutant; and mutant
```

toxin-deficient Aspergillus sp. (61pp)

=> file registry
COST IN U.S. DOLLARS — SINCE FILE ENTRY: 10.46 — TOTAL SESSION: 10.67

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 16:57:37 ON 29 JUL 2004
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 28 JUL 2004 HIGHEST RN 718597-29-6
DICTIONARY FILE UPDATES: 28 JUL 2004 HIGHEST RN 718597-29-6

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

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Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

```
=> s dimethylallyl-cycloacetoacetyl-L-tryptophan synthase
           810 DIMETHYLALLYL
             2 CYCLOACETOACETYL
       1568416 L
         34465 TRYPTOPHAN
         25801 SYNTHASE
L2           0 DIMETHYLALLYL-CYCLOACETOACETYL-L-TRYPTOPHAN SYNTHASE
                 (DIMETHYLALLYL(W)CYCLOACETOACETYL(W)L(W)TRYPTOPHAN(W)SYNTHASE)

=> s dimethylallyl-cycloacetoacetyl tryptophan synthase
           810 DIMETHYLALLYL
             2 CYCLOACETOACETYL
         34465 TRYPTOPHAN
         25801 SYNTHASE
L3           1 DIMETHYLALLYL-CYCLOACETOACETYL TRYPTOPHAN SYNTHASE
                 (DIMETHYLALLYL(W)CYCLOACETOACETYL(W)TRYPTOPHAN(W)SYNTHASE)

=> d l3

L3   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   280784-57-8  REGISTRY
CN   DNA (Aspergillus oryzae strain A1560 gene DCAT-S
     dimethylallylcycloacetoacetyltryptophan synthase cDNA plus flanks)
     (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   1: PN: WO0039322 SEQID: 1 claimed DNA
FS   NUCLEIC ACID SEQUENCE
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, TOXCENTER, USPATFULL
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  BIOL (Biological study); OCCU (Occurrence); PROC
       (Process); PRP (Properties)
```

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**RELATED SEQUENCES AVAILABLE WITH SEQLINK**

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
*** USE 'SQD' OR 'SQIDE' FORMATS TO DISPLAY SEQUENCE ***
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)


=> s  dimethylallylcycloacetoacetyltryptophan synthase
             2 DIMETHYLALLYLCYCLOACETOACETYLTRYPTOPHAN
         25801 SYNTHASE
L4           1 DIMETHYLALLYLCYCLOACETOACETYLTRYPTOPHAN SYNTHASE
                 (DIMETHYLALLYLCYCLOACETOACETYLTRYPTOPHAN(W)SYNTHASE)

=> file medline hcaplus biosis biotechds scisearch embase
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                  ENTRY    SESSION
FULL ESTIMATED COST                               52.18      62.85

FILE 'MEDLINE' ENTERED AT 16:59:46 ON 29 JUL 2004

FILE 'HCAPLUS' ENTERED AT 16:59:46 ON 29 JUL 2004
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FILE 'BIOTECHDS' ENTERED AT 16:59:46 ON 29 JUL 2004
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=> s  dimethylallylcycloacetoacetyltryptophan synthase
L5           1 DIMETHYLALLYLCYCLOACETOACETYLTRYPTOPHAN SYNTHASE

=> d l5 ibib ab

L5   ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2000:457232  HCAPLUS
DOCUMENT NUMBER:          133:85094
TITLE:                    Protein production in Aspergillus mutant cells that
                          produce decreased levels of toxin
INVENTOR(S):              Christensen, Bjorn Eggert; Mollgaard, Henrik;
                          Kaasgaard, Svend; Lehmbeck, Jan
PATENT ASSIGNEE(S):       Novo Nordisk A/S, Den.
SOURCE:                   PCT Int. Appl., 66 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     WO 2000039322      A1   20000706       WO 1999-DK726    19991222
         W:  AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
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            MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
            SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ,
            BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
            DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
            CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
    EP 1141371        A1   20011010       EP 1999-960956   19991222
        R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
            IE, SI, LT, LV, FI, RO
    JP 2002533133     T2   20021008       JP 2000-591212   19991222
    US 6383781        B1   20020507       US 1999-472364   19991223
    US 2002197682     A1   20021226       US 2002-99704    20020315
PRIORITY APPLN. INFO.:                  DK 1998-1726     A  19981223
                                        DK 1999-745      A  19990527
                                        US 1999-117396P  P  19990127
                                        US 1999-139593P  P  19990617
                                        WO 1999-DK726    W  19991222
                                        US 1999-472364   A3 19991223
AB  A method is provided for producing a polypeptide of interest by (a)
    cultivating a mutant of a parent Aspergillus cell, wherein (i) the mutant
    comprises a first nucleic acid sequence encoding the polypeptide and a
    second nucleic acid sequence comprising a modification of at least one of
    the genes responsible for the biosynthesis or secretion of at least one
    toxin, and (ii) the mutant produces less of the toxin than the parent
    Aspergillus cell when cultured under the same conditions; and (b)
    isolating the polypeptide from the culture medium.  Also, mutants of
    Aspergillus cells are provided, as well as methods for obtaining the
    mutant cells.  Thus, the dimethylallylcycloacetoacetyl-L-tryptophan
    synthase gene (DCAT-S) was characterized in Aspergillus oryzae.  Since
    this enzyme is involved in biosynthesis of cyclopiazonic acid (CPA),
    CPA-neg. strains were constructed by modification of the DCAT-S gene, and
    improved of lipase and xylanase genes was obsd. in the CPA-neg. strains.
    Strains lacking genes aflR and omtA, involved in aflatoxin biosynthesis,
    also demonstrated improved heterologous protein prodn.
REFERENCE COUNT:          4     THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                                RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=>  dimethylallylcycloacetoacety synthase
DIMETHYLALLYLCYCLOACETOACETY IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s dimethylallylcycloacetoacety synthase
L6            0 DIMETHYLALLYLCYCLOACETOACETY SYNTHASE

=> s dimethylallyl cycloacetoacety  l-tryptophan synthase
L7            0 DIMETHYLALLYL CYCLOACETOACETY L-TRYPTOPHAN SYNTHASE

=> s Aspergillus oryzae and synthase
L8          125 ASPERGILLUS ORYZAE AND SYNTHASE

=> dup rem l8
PROCESSING COMPLETED FOR L8
L9           62 DUP REM L8 (63 DUPLICATES REMOVED)

=> s l9 and  dimethylallylcycloacetoacetyltryptophan synthase
L10           1 L9 AND DIMETHYLALLYLCYCLOACETOACETYLTRYPTOPHAN SYNTHASE

=> d his

     (FILE 'HOME' ENTERED AT 16:56:06 ON 29 JUL 2004)

     FILE 'MEDLINE, HCAPLUS, BIOSIS, BIOTECHDS, SCISEARCH, EMBASE' ENTERED AT
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     16:56:45 ON 29 JUL 2004
L1             1 S DIMETHYLALLYL-CYCLOACETOACETYL-L-TRYPTOPHAN SYNTHASE

     FILE 'REGISTRY' ENTERED AT 16:57:37 ON 29 JUL 2004
L2             0 S DIMETHYLALLYL-CYCLOACETOACETYL-L-TRYPTOPHAN SYNTHASE
L3             1 S DIMETHYLALLYL-CYCLOACETOACETYL TRYPTOPHAN SYNTHASE
L4             1 S  DIMETHYLALLYLCYCLOACETOACETYLTRYPTOPHAN SYNTHASE

     FILE 'MEDLINE, HCAPLUS, BIOSIS, BIOTECHDS, SCISEARCH, EMBASE' ENTERED AT
     16:59:46 ON 29 JUL 2004
L5             1 S  DIMETHYLALLYLCYCLOACETOACETYLTRYPTOPHAN SYNTHASE
L6             0 S DIMETHYLALLYLCYCLOACETOACETY SYNTHASE
L7             0 S DIMETHYLALLYL CYCLOACETOACETY  L-TRYPTOPHAN SYNTHASE
L8           125 S ASPERGILLUS ORYZAE AND SYNTHASE
L9            62 DUP REM L8 (63 DUPLICATES REMOVED)
L10            1 S L9 AND  DIMETHYLALLYLCYCLOACETOACETYLTRYPTOPHAN SYNTHASE

=> s l9 and  tryptophan synthase
L11            2 L9 AND TRYPTOPHAN SYNTHASE

=> d l11 1-2 ibib ab

L11  ANSWER 1 OF 2     MEDLINE on STN
ACCESSION NUMBER:    96358132     MEDLINE
DOCUMENT NUMBER:     PubMed ID: 8762144
TITLE:               Invariant glycines and prolines flanking in loops the
                     strand beta 2 of various (alpha/beta)8-barrel enzymes: a
                     hidden homology?.
AUTHOR:              Janecek S
CORPORATE SOURCE:    Institute of Ecobiology, Slovak Academy of Sciences,
                     Bratislava, Slovakia.. sjanecek@ue.savba.sk
SOURCE:              Protein science : a publication of the Protein Society,
                     (1996 Jun) 5 (6) 1136-43.
                     Journal code: 9211750. ISSN: 0961-8368.
PUB. COUNTRY:        United States
DOCUMENT TYPE:       Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:            English
FILE SEGMENT:        Priority Journals
ENTRY MONTH:         199612
ENTRY DATE:          Entered STN: 19970128
                     Last Updated on STN: 19980206
                     Entered Medline: 19961213
AB   The question of parallel (alpha/beta)8-barrel fold evolution remains
     unclear, owing mainly to the lack of sequence homology throughout the
     amino acid sequences of (alpha/beta)8-barrel enzymes.  The "classical"
     approaches used in the search for homologies among (alpha/beta)8-barrels
     (e.g., production of structurally based alignments) have yielded
     alignments perfect from the structural point of view, but the approaches
     have been unable to reveal the homologies.  These are proposed to be
     "hidden" in (alpha/beta)8-barrel enzymes.  The term "hidden homology"
     means that the alignment of sequence stretches proposed to be homologous
     need not be structurally fully satisfactory.  This is due to the very long
     evolutionary history of all (alpha/beta)8-barrels.  This work identifies
     so-called hidden homology around the strand beta 2 that is flanked by
     loops containing invariant glycines and prolines in 17 different
     (alpha/beta)8-barrel enzymes, i.e., roughly in half of all currently known
     (alpha/beta)8-barrel proteins.  The search was based on the idea that a
     conserved sequence region of an (alpha/beta)8-barrel enzyme should be more
     or less conserved also in the equivalent part of the structure of the
     other enzymes with this folding motif, given their mutual evolutionary
     relatedness.  For this purpose, the sequence region around the
     well-conserved second beta-strand of alpha-amylase flanked by the
     invariant glycine and proline (56_GFTAIWITP, Aspergillus
     oryzae alpha-amylase numbering), was used as the
     sequence-structural template.  The proposal that the second beta-strand of
```

(alpha/beta)8-barrel fold is important from the evolutionary point of view is strongly supported by the increasing trend of the observed beta 2-strand structural similarity for the pairs of (alpha/beta)8-barrel enzymes: alpha-amylase and the alpha-subunit of **tryptophan synthase**, alpha-amylase and mandelate racemase, and alpha-amylase and cyclodextrin glycosyltransferase. This trend is also in agreement with the existing evolutionary division of the entire family of (alpha/beta)8-barrel proteins.

L11 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:457232 HCAPLUS
DOCUMENT NUMBER: 133:85094
TITLE: Protein production in Aspergillus mutant cells that produce decreased levels of toxin
INVENTOR(S): Christensen, Bjorn Eggert; Mollgaard, Henrik; Kaasgaard, Svend; Lehmbeck, Jan
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000039322	A1	20000706	WO 1999-DK726	19991222
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1141371	A1	20011010	EP 1999-960956	19991222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533133	T2	20021008	JP 2000-591212	19991222
US 6383781	B1	20020507	US 1999-472364	19991223
US 2002197682	A1	20021226	US 2002-99704	20020315

PRIORITY APPLN. INFO.:

DK 1998-1726	A	19981223
DK 1999-745	A	19990527
US 1999-117396P	P	19990127
US 1999-139593P	P	19990617
WO 1999-DK726	W	19991222
US 1999-472364	A3	19991223

AB A method is provided for producing a polypeptide of interest by (a) cultivating a mutant of a parent Aspergillus cell, wherein (i) the mutant comprises a first nucleic acid sequence encoding the polypeptide and a second nucleic acid sequence comprising a modification of at least one of the genes responsible for the biosynthesis or secretion of at least one toxin, and (ii) the mutant produces less of the toxin than the parent Aspergillus cell when cultured under the same conditions; and (b) isolating the polypeptide from the culture medium. Also, mutants of Aspergillus cells are provided, as well as methods for obtaining the mutant cells. Thus, the dimethylallylcycloacetoacetyl-L-**tryptophan synthase** gene (DCAT-S) was characterized in **Aspergillus oryzae**. Since this enzyme is involved in biosynthesis of cyclopiazonic acid (CPA), CPA-neg. strains were constructed by modification of the DCAT-S gene, and improved of lipase and xylanase genes was obsd. in the CPA-neg. strains. Strains lacking genes aflR and omtA, involved in aflatoxin biosynthesis, also demonstrated improved heterologous protein prodn.

```
REFERENCE COUNT:          4      THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT


=> d his

     (FILE 'HOME' ENTERED AT 16:56:06 ON 29 JUL 2004)

     FILE 'MEDLINE, HCAPLUS, BIOSIS, BIOTECHDS, SCISEARCH, EMBASE' ENTERED AT
     16:56:45 ON 29 JUL 2004
L1             1 S DIMETHYLALLYL-CYCLOACETOACETYL-L-TRYPTOPHAN SYNTHASE

     FILE 'REGISTRY' ENTERED AT 16:57:37 ON 29 JUL 2004
L2             0 S DIMETHYLALLYL-CYCLOACETOACETYL-L-TRYPTOPHAN SYNTHASE
L3             1 S DIMETHYLALLYL-CYCLOACETOACETYL TRYPTOPHAN SYNTHASE
L4             1 S  DIMETHYLALLYLCYCLOACETOACETYLTRYPTOPHAN SYNTHASE

     FILE 'MEDLINE, HCAPLUS, BIOSIS, BIOTECHDS, SCISEARCH, EMBASE' ENTERED AT
     16:59:46 ON 29 JUL 2004
L5             1 S  DIMETHYLALLYLCYCLOACETOACETYLTRYPTOPHAN SYNTHASE
L6             0 S DIMETHYLALLYLCYCLOACETOACETY SYNTHASE
L7             0 S DIMETHYLALLYL CYCLOACETOACETY  L-TRYPTOPHAN SYNTHASE
L8           125 S ASPERGILLUS ORYZAE AND SYNTHASE
L9            62 DUP REM L8 (63 DUPLICATES REMOVED)
L10            1 S L9 AND  DIMETHYLALLYLCYCLOACETOACETYLTRYPTOPHAN SYNTHASE
L11            2 S L9 AND  TRYPTOPHAN SYNTHASE

=> log y
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                      ENTRY    SESSION
FULL ESTIMATED COST                                   16.45      79.30

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                      ENTRY    SESSION
CA SUBSCRIBER PRICE                                   -1.47      -1.47

STN INTERNATIONAL LOGOFF AT 17:04:34 ON 29 JUL 2004
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First Hit Fwd Refs Previous Doc Next Doc Go to Doc#

End of Result Set

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L1: Entry 1 of 1 File: USPT May 7, 2002

US-PAT-NO: 6383781
DOCUMENT-IDENTIFIER: US 6383781 B1

TITLE: Methods for producing polypeptides in aspergillus mutant cells

DATE-ISSUED: May 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Christensen; Bjorn Eggert	Bagsvaerd			DK
Mollgaard; Henrik	Lyngby			DK
Kaasgaard; Svend	Soborg			DK
Lehmbeck; Jan	Vekso			DK

ASSIGNEE-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY	TYPE CODE
Novozymes A/S	Bagsvaerd			DK	03

APPL-NO: 09/ 472364 [PALM]
DATE FILED: December 23, 1999

PARENT-CASE:
CROSS-REFERENCE TO RELATED APPLICATIONS This application claims benefit to U.S. provisional application No. 06/117,396 filed on Jan. 27, 1999, and U.S. provisional application No. 60/139,593 filed on Jun. 17, 1999, and claims foreign priority under 35 U.S.C. 119 to Danish application no. PA 1998 01726 filed on Dec. 23, 1998, Danish application no. DA 1999 00745 filed on May 27, 1999, the contents of which are fully incorporated herein by reference.

FOREIGN-APPL-PRIORITY-DATA:

COUNTRY	APPL-NO	APPL-DATE
DK	1998 01726	December 23, 1998
DK	1999 00745	May 27, 1999

INT-CL: [07] C12 P 21/06, C12 N 1/14

US-CL-ISSUED: 435/69.1; 435/71.1, 435/71.2, 435/256.1
US-CL-CURRENT: 435/69.1; 435/256.1, 435/71.1, 435/71.2

FIELD-OF-SEARCH: 435/69.1, 435/71.1, 435/71.2, 435/172.3, 435/320.1, 435/252.3, 435/256.1

PRIOR-ART-DISCLOSED:

U.S. PATENT DOCUMENTS

Search Selected | Search ALL | Clear

	PAT-NO	ISSUE-DATE	PATENTEE-NAME	US-CL
☐	5958727	September 1999	Brody et al.	435/69.1

FOREIGN PATENT DOCUMENTS

FOREIGN-PAT-NO	PUBN-DATE	COUNTRY	US-CL
1271068	January 1994	SU	
WO 95/15390	June 1995	WO	
WO 95/15391	June 1995	WO	

OTHER PUBLICATIONS

Abstract of article by Tudzynski et al., Mol Gen Genet, vol. 261, pp. 133-141 (1999).
Abstract of Russian Patent No. SU 1271068 A1.

ART-UNIT: 1653

PRIMARY-EXAMINER: Carlson; Karen Cochrane

ATTY-AGENT-FIRM: Lambiris; Elias Garbell; Jason

ABSTRACT:

A method is provided for producing a polypeptide of interest by (a) cultivating a mutant of a parent Aspergillus cell, wherein (i) the mutant comprises a first nucleic acid sequence encoding the polypeptide and a second nucleic acid sequence comprising a modification of at least one of the genes responsible for the biosynthesis or secretion of at least one toxin, and (ii) the mutant produces less of the toxin than the parent Aspergillus cell when cultured under the same conditions; and (b) isolating the polypeptide from the culture medium. Also, mutants of Aspergillus cells are provided, as well as methods for obtaining the mutant cells.

17 Claims, 2 Drawing figures

Previous Doc Next Doc Go to Doc#

First Hit Fwd Refs Previous Doc Next Doc Go to Doc#

End of Result Set

Generate Collection Print

L1: Entry 1 of 1 File: USPT May 7, 2002

US-PAT-NO: 6383781
DOCUMENT-IDENTIFIER: US 6383781 B1

TITLE: Methods for producing polypeptides in aspergillus mutant cells

DATE-ISSUED: May 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Christensen; Bjorn Eggert	Bagsvaerd			DK
Mollgaard; Henrik	Lyngby			DK
Kaasgaard; Svend	Soborg			DK
Lehmbeck; Jan	Vekso			DK

US-CL-CURRENT: 435/69.1; 435/256.1, 435/71.1, 435/71.2

CLAIMS:

What is claimed is:

1. A method for producing a polypeptide, said method comprising:

(a) cultivating a mutant of a parent Aspergillus cell, wherein (i) the mutant comprises a nucleic acid sequence encoding said polypeptide, and (ii) the mutant produces less of at least one toxin selected from the group consisting of emodin, kojic acid, malformin, 3-nitropropionic acid, ochratoxins, and secalonic acids than the parent Aspergillus cell when cultured under the same conditions; and

(b) isolating the polypeptide from the culture medium.

2. The method of claim 1, wherein the mutant produces at least 90% less of the toxin than the parent Aspergillus cell when cultured under the same conditions.

3.The method of claim 1, wherein the toxin is emodin.

4. The method of claim 1, wherein the toxin is kojic acid.

5. The method of claim 1, wherein the toxin is malformin.

6. The method of claim 1, wherein the toxin is 3-nitropropionic acid.

7. The method of claim 1, wherein the toxin is an ochratoxin.

8. The method of claim 1, wherein the toxin is a secalonic acid.

9. The method of claim 1, wherein the mutant produces less of at least two said toxins than the parent Aspergillus cell when cultured under the same conditions.

10. The method of claim 1, wherein the mutant additionally produces less of an aflatoxin.

11. The method of claim 1, wherein the mutant additionally produces less of a cyclopiazonic acid.

12. The method of claim 1, wherein the parent Aspergillus cells is a cell from a subgroup selected from the group consisting of Chaetosartorya, Emericella, Eurotium, Fenellia, Hemicarpenteles, Neosartorya, Petromyces, Satoia, and Sclerocleista.

13. The method of claim 1, wherein the polypeptide of interest is native to the Aspergillus cell.

14. The method of claim 13, wherein the amount of the polypeptide produced by the mutant is greater than the amount produced by the parent Aspergillus cell when cultured under the same conditions.

15. The method of claim 1, wherein the polypeptide is heterologous to the mutant.

16. The method of claim 1, wherein the polypeptide is selected from the group consisting of a hormone or a precursor thereof, an enzyme or an enzyme variant or a precursor thereof, an antibody or a functional fragment thereof, a receptor or a functional fragment thereof, and a reporter.

17. The method of claim 16, wherein the polypeptide is selected from the group consisting of aminopeptidase, alpha-galactosidase, alpha-glucosidase, amylase, beta-galactosidase, beta-glucosidase, carbohydrase, carboxypeptidase, catalase, cellulase, chitinase, cutinase, cyclodextrin glycosyltransferase, deoxyribonuclease, endo-peptidase, exo-peptidase, esterase, galactanase, glucoamylase, invertase, laccase, lipase, lyase, mannase, mannosidase, mutanase, oxidase, oxygenase, pectate lyase, pectinase, peroxidase, phytase, polyphenoloxidase, protease, ribonuclease, transglutaminase, and xylanase.

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☐ 1. Document ID: US 20020197682 A1

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L1: Entry 1 of 3 File: PGPB Dec 26, 2002

PGPUB-DOCUMENT-NUMBER: 20020197682
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020197682 A1

TITLE: Methods for producing polypeptides in Aspergillus mutant cells

PUBLICATION-DATE: December 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Christensen, Bjorn Eggert	Bagsvaerd		DK	
Mollgaard, Henrik	Lyngby		DK	
Kaasgaard, Svend	Soborg		DK	
Lehmbeck, Jan	Vekso		DK	

US-CL-CURRENT: 435/71.1; 435/254.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 2. Document ID: US 6383781 B1

L1: Entry 2 of 3 File: USPT May 7, 2002

US-PAT-NO: 6383781
DOCUMENT-IDENTIFIER: US 6383781 B1

TITLE: Methods for producing polypeptides in aspergillus mutant cells

DATE-ISSUED: May 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Christensen; Bjorn Eggert	Bagsvaerd			DK
Mollgaard; Henrik	Lyngby			DK
Kaasgaard; Svend	Soborg			DK
Lehmbeck; Jan	Vekso			DK

US-CL-CURRENT: 435/69.1; 435/256.1, 435/71.1, 435/71.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

☐ 3. Document ID: US 20020197682 A1, WO 200039322 A1, AU 200017740 A, EP 1141371 A1, CN 1333837 A, US 6383781 B1, JP 2002533133 W

L1: Entry 3 of 3 File: DWPI Dec 26, 2002

DERWENT-ACC-NO: 2000-452411
DERWENT-WEEK: 200304

TITLE: Producing a polypeptide of interest such as a hormone or enzyme, comprising cultivating a mutant of a parent Aspergillus cell which produces less of at least one toxin of interest compared to the parent cell under the same conditions

INVENTOR: CHRISTENSEN, B E; KAASGAARD, S ; LEHMBECK, J ; MOLLGAARD, H

PRIORITY-DATA: 1999DK-0000745 (May 27, 1999), 1998DK-0001726 (December 23, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 20020197682 A1	December 26, 2002		000	C12P021/02
WO 200039322 A1	July 6, 2000	E	061	C12P021/00
AU 200017740 A	July 31, 2000		000	C12P021/00
EP 1141371 A1	October 10, 2001	E	000	C12P021/00
CN 1333837 A	January 30, 2002		000	C12P021/00
US 6383781 B1	May 7, 2002		000	C12P021/06
JP 2002533133 W	October 8, 2002		061	C12N015/09

INT-CL (IPC): C12 N 1/14; C12 N 1/15; C12 N 1/16; C12 N 9/00; C12 N 9/10; C12 N 9/20; C12 N 9/42; C12 N 9:10; C12 N 15/01; C12 N 15/09; C12 P 21/00; C12 P 21/02; C12 P 21/06; C12 P 21:00; C12 R 1:66; C12 N 1/15; C12 R 1:69; C12 R 1:66; C12 R 1:66; C12 P 21/00; C12 N 9/10

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw De

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☐	L2	435/193.ccls.	1906
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